PEDIATRIC KIDNEY TRANSPLANT

Surgical Specialty:	Transplant Surgery
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Background:

- General Considerations[1–3]
  - The underlying etiology of end-stage renal disease (ESRD) in children is significantly different from ESRD in adults. Most commonly, it is caused by congenital anomalies of the kidney and urinary tract followed by focal segmental glomerulosclerosis (FSGS) and glomerulonephritis.[4]
  - Pediatric surgical techniques vary depending on the child's size and the underlying pathology. Pediatric donor kidneys are rare. Thus adult-sized kidneys (ASK) are often used. Depending on the child's size, the surgical technique may vary substantially.[5]
    - In patients <10 kg, an intraperitoneal approach is preferred. This involves is a midline incision with ASK placed on the right side of the abdomen after transposition of the bowels medially to expose the common iliac vessels, inferior vena cava, and aorta.
    - In patients >15 kg, an extraperitoneal approach is preferred. This involves a right-or left-sided abdominal incision with mobilization of the peritoneum to expose the posterior abdominal wall and its vessels.
- Patient Considerations
  - Patients may have genetic syndromes or congenital defects with urologic involvement, and therefore, may have had numerous previous surgeries.
  - Cardiac death is the leading cause of death in children post-transplant. Therefore, a formal evaluation of the patient's cardiac function must be performed prior to surgery.
    - ESRD increases the risk of coronary artery disease, hypertension, pericarditis, arrhythmias, left ventricular hypertrophy, and diastolic cardiomyopathy.
    - Congestive heart failure should always be considered in the setting of hypertension, volume overload status, profound uremia, or a history of pericarditis.
    - Large fluid volumes are required during the induction phase of the operation, and the heart will need to tolerate the additional volume without developing congestive cardiac failure.
  - Multifactorial hypertension is common from stiff arteries, the hyperreninemic response, or increased cardiac output to compensate for anemia.

- Anemia should be optimized without a transfusion preoperatively due to the risk of HLA sensitization before transplant. Post-transplant leuko-reduced PRBCs should be used.
- Nutritional status may be impaired, and the patients may be fed via a nasogastric or gastrostomy tube. Uremia is known to cause nausea.
- Electrolyte derangements, specifically hyperkalemia, from ESRD and hypercalcemia and hypercalciuria may be the result of uncontrolled secondary hyperparathyroidism.
- Slowed growth, nutritional insufficiency, and long-term steroid use often result in cognitive delays, bone growth delays, and overall impaired development.

Anesthetic Planning:

- Pre-Anesthetic Evaluation[1–3]
  - Additional labs/tests indicated during work-up
    - Assessment for hemodynamic stability and active infection, which is a contraindication for transplantation.
    - Assessment of pre-transplantation urine output.
    - Prior to and on the day of surgery, hyperkalemia (K+ >6.0 mmol/L), acidosis, or volume overload should be treated before proceeding.
    - Cardiovascular assessment includes history, physical exam, electrocardiogram (EKG), and echocardiogram. If any abnormal findings are present, obtain a cardiology consult.
    - A history of fractures or bone disease due to hypocalcemia can be a risk factor for dental injury during intubation.
    - Full stomach precautions are usually needed as organ availability is unpredictable, and additionally, delayed gastric emptying is common in children with renal failure. If present, nasogastric tubes should be suctioned.
    - Assessment of vascular access should occur preoperatively as ultrasound-guided PIV placement may be required.
    - Confirm and document arteriovenous (AV) shunt patency in the preoperative and immediate postoperative phase.
  - Living-related kidney transplant
    - Clear communication preoperatively with the donor team after finishing the preoperative evaluation is critical.
- Specific or Unique Room Set-Up Requirements
  - Airway
    - All patients will require an oral endotracheal tube (OETT), and multiple smaller sizes should be available. A video laryngoscope or pediatric fiberoptic scope should be readily available.
  - Drugs/Infusions
    - Drugs that are renally metabolized or have metabolites that are renally metabolized, have nephrotoxic profiles, or can cause potassium shifts should be avoided. Additionally, post-transplant return of renal function is not immediate, and the same considerations should be taken with additional dose adjustments for changes in protein-binding and volume of distribution.
    - Induction Therapy for Transplant:
      - Antithymocyte Globulin (Thymoglobulin) (T-Cell Antibodies)
        - Accounts for >60% of induction agents and are polyclonal antibodies against human T-lymphocyte antigens.

        - Infusion is typically started at the time of anesthesia induction in the operating room (OR), and definitively started before the reperfusion of the transplanted kidney.
        - Thymoglobulin dosing (1.5 mg/kg) may be repeated in the postoperative period. Alternatively, 5 mg/kg may be administered over 12 hours.
    - Basiliximab (Simulect) (Interleukin-2 Receptor Antibodies)
        - Accounts for 30-40% of induction agents and is a monoclonal anti-CD25 antibody used to stop T-cell proliferation without affecting T lymphocyte levels.
        - Needs to be given 2 hours prior to surgery.
        - Basiliximab dosing for patients <35 kg is 10 mg. For patients ≥ 35 kg, administer 20 mg.
    - Alemtuzumab (Campath) (Monoclonal antibody)
        - Accounts for an unknown percentage of induction agents, usage is reportedly similar to basiliximab in 2022.
        - Monoclonal antibody against CD52 present on T and B cell monocytes, and natural killer cells.
    - All induction agents, particularly thymoglobulin and campath, cause cytokine release and can cause varying levels of reactions, including fever, chills and rigors. The standard of care is to pretreat with acetaminophen (10 mg/kg), methylprednisolone (2.5 mg/kg), and diphenhydramine (2.5 mg/kg).
    - These medications are typically prepared by the pharmacy. They require confirmation preoperatively on the day of surgery. The surgery should be delayed if the above medications are not in the OR at surgical timeout.
- Induction of Anesthesia Agents
    - Anxiolysis with midazolam is acceptable. Most patients have an IV access for induction. Propofol is the most commonly used induction agent. Neuromuscular blockade with succinylcholine (2 mg/kg), rocuronium (0.6 mg/kg), or cisatracurium (0.15 mg/kg) may be used. Rocuronium is now the preferred agent due to the availability of sugammadex for reversal. Succinylcholine may be contraindicated depending on the potassium level.
    - The preferred opioids are fentanyl (inactive metabolites) or remifentanil due to esterase-dependent elimination. We recommend the avoidance of morphine and meperidine.
- Maintenance of Anesthesia Agents

  A propofol infusion (100-300 mcg/kg/min) is equivocal to volatile anesthetic agents. Prolonged nitrous oxide use is relatively contraindicated due to intestinal distension impacting closure. Regional anesthesia (transversus abdominal plane (TAP) or quadratus lumborum (QL) blocks) or neuraxial anesthesia (thoracic epidural) can reduce maintenance requirements. The limiting factor for neuraxial anesthetics is the coagulation status and platelet dysfunction.
- PONV Prophylaxis
    - Ondansetron (0.1-0.15mg/kg to a maximum of 4mg)
- Fluid management in pediatric kidney transplant

- Baseline electrolytes should be obtained, and fluid choice should be administered based on electrolyte findings. Plasmalyte is the fluid of choice. However, if lactated Ringer's solution is used, consideration should be given to the potassium (4mEq/L) that it contains. If sodium chloride is used, consideration should be given to the baseline sodium levels and the rate of correction, and the potential for a hyperchloremic hypernatremic metabolic acidosis.
- 5% albumin
    - There is no difference in outcomes between crystalloid and colloid solutions for resuscitation. Achieving an adequate central venous pressure (CVP) may require large volumes of crystalloid administration. Therefore, to reduce fluid shifts into the extracellular space, colloids and/or PRBCs are often required.

▪ Vasopressors
- Norepinephrine (0.03mcg/kg/min) is the first-line vasopressor and can be titrated to effect.[6] Dopamine is no longer recommended. It was previously thought to provide renal protection, but this has not been backed by evidence.[7]
- Vasopressin (0.5 milliunits/kg/hour) infusion is now considered the second line agent. A small bolus test dose before infusion is accepted practice. In patients on angiotensin-converting-enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), vasopressin may be the most effective choice.
- We do not recommend using phenylephrine infusions because of the risk of unopposed alpha-1 constriction, and its use has been reported as an independent factor for delayed graft function.[8]

▪ Diuresis Agents
- After transplantation and completion of the anastomoses, furosemide (1 mg/kg) and/or mannitol (0.5-1 g/kg) are used to promote diuresis.
- Mannitol administration is typically used as an infusion with a filter.

▪ Acidemia Attenuation
- Sodium bicarbonate 75 mEq/L in 0.45% NS (1-2 mEq/kg) as a bolus prior to aortic unclamping or immediately afterwards.

▪ Heparinization
- If the aorta and/or inferior vena cava are cross-clamped, low-dosage heparinization (50 to 100 Units/kg) is often used.

o Monitors
▪ Standard American Society of Anesthesiologists monitors.
▪ If the patient has a previous AV shunt, the noninvasive blood pressure (BP) cuff must be placed on a different limb.
▪ Neuromuscular blockade monitoring
▪ Younger patients are more predisposed to severe fluid shifts and are subsequently at a much higher risk of graft hypoperfusion. Arterial line placement is often indicated for this reason. If the patient has a previous AV shunt, then careful selection of the arterial line site to protect the shunt must occur.
▪ Central venous catheter (CVC) placement is indicated most often for specific induction agents. Other indications include damaged peripheral vasculature and small-sized children receiving an adult kidney. The higher cardiac output

(CO) required by the adult kidney in a child can make mean arterial pressure (MAP) goals difficult to maintain, and, in these cases, additional monitoring of CVP in the setting of a large amount of fluid administration can be helpful.
        - Consider using preexisting lines such as PICC or Hickman catheter.
        - At least one large bore PIV on a fluid warmer should be available.
    - Blood Availability
        - Preoperative anemia is very common. Therefore, two units of leuko-reduced red blood cells should be prepared.
        - Infants receiving an adult donor kidney should have PRBCs present in the room and additional blood available. The adult kidney requires a higher CO to perfuse the organ, predisposing the new graft to hypoperfusion.
    - PICU Bed Availability
        - These patients should be monitored in the PICU postoperatively.
        - Most children can be extubated in the operating room. An exception to this is infants with large volume resuscitation needs may require delayed extubation, or patients who develop pulmonary edema.

Intraoperative Considerations:

- General[1–3,6]
    - OETT, two PIV lines, arterial line, +/- CVC, ASA standard monitors, and foley catheter.
- Induction
    - IV or inhalation induction typically with neuromuscular blockade.
- Positioning
    - Supine with both arms out at <90 degrees.
    - Access to the AVF site if this exists.
- Maintenance
    - Isoflurane/sevoflurane, fentanyl, and rocuronium or cisatracurium for neuromuscular blockade.
    - Lung protective ventilation (tidal volumes 6-8 ml/kg, postoperative end-expiratory pressure 5-10 cm H_20)
- Hemodynamic/Physiologic goals
    - Prior to the start of surgery, a team discussion with the surgeon should occur regarding MAP goals. MAP goals will vary depending on size of the child, size of the donor organ, and preoperative BPs of both the organ donor and recipient.
    - General guidelines include :
        - If a CVC is present and CVP can be measured, target a CVP range from 12-14 mm Hg prior to reperfusion and 10-12 mm Hg post-reperfusion.
        - MAP goals of 70 mm Hg are usually required and achieved by a combination of fluid loading and vasopressor use.
        - If vasopressors are used, see the above recommendations for infusions
        - If bolus vasopressor dosing is required, younger children may require heart rate (HR) support along with BP support. We suggest ephedrine (0.1 mg/kg), epinephrine (0.5-1 mcg/kg). Phenylephrine boluses are acceptable as well, however, infusions are not recommended, as stated above.
        - Unique to pediatrics, calcium chloride 10 mg/kg can be used for hemodynamic support. The most common time intraoperatively to require this is after cross-clamp release to stabilize the myocardium if large amounts of potassium are freed in the absence of organ flushing before reperfusion.
- Surgical Considerations

    - Since neuromuscular blockers are commonly used, monitoring of neuromuscular blockade is recommended.
    - Timing of induction agents should be discussed.
    - Mannitol and furosemide should be available.
    - Fluid loading before reperfusion.
    - Aortic clamping and unclamping
        - Size discrepancies between the transplanted organ and the patient may necessitate aortic clamping and unclamping to facilitate the completion of the anastomosis and limit blood sequestration. This can cause acidosis and worsen an already deranged acid-base status. Attenuation of this can be achieved with sodium bicarbonate.
- Emergence/Disposition
    - Variable, depending on extubation in the OR vs the PICU.
    - Ensure adequate reversal of neuromuscular blockade.
    - Postoperative TAP, ESP, QL block, or epidural catheter for postoperative analgesia.
- Post-op Care
    - The most critical portion of postoperative care is maintenance of blood volume and BP to perfuse the graft.
    - Measurement of urine output is vital, and immediate replacement should occur in real-time.
    - Typically, urine output is replaced milliliter for milliliter with half-normal saline for the first two days post-transplant.
    - The greatest risk factor for graft failure is graft hypoperfusion and acute tubular necrosis (ATN), both of which can be avoided by volume expansion, careful measurement of volume status, and vasopressor support if required to maintain adequate MAPs.
    - Postoperative pain management:
        - IV opioids
        - Epidural analgesia after careful evaluation of the coagulation status.

Case-Specific Complications/Pitfalls

- Mild pulmonary edema due to fluid overloading has been reported in up to 25% of patients.
- Reperfusion is when the most hemodynamic instability is likely to occur, especially in younger children receiving ASKs. Open communication with the surgical team with ideally 5-minute and 1-minute warnings can help attenuate the response. Adequate preload and the use of vasopressors and calcium during unclamping may be necessary.
- Vascular thrombosis is a cause of graft failure in infants that can be prevented by management of reperfusion.
- Delayed graft function, defined as requiring dialysis within a week post-transplant, may occur postoperatively.

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